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DRUG INDUSTRY ANTITRUST ACT

HEARINGS

BEFORE THE

SUBCOMMITTEE ON ANTITRUST AND MONOPOLY

OF THE

COMMITTEE ON THE JUDICIARY

UNITED STATES SENATE

EIGHTY-SEVENTH CONGRESS

FIRST SESSION

PURSUANT TO

S. Res. 52

ON

S. 1552

A BILL TO AMEND AND SUPPLEMENT THE ANTITRUST LAWS, WITH RESPECT TO THE MANUFACTURE AND DISTRIBUTION OF DRUGS, AND FOR OTHER PURPOSES

PART 2

A.M.A. and Medical Authorities

(Appendix)

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EXHIBITS AND APPENDIX [1]

[1] Exhibits below p. 459 may be found in pt. 1.

*Exhibit 35 was not provided.

OTHER MATERIAL

PREPARED STATEMENTS

EXHIBITS AND APPENDIX

EXHIBIT 1

NATIONAL ACADEMY OF SCIENCES - NATIONAL RESEARCH COUNCIL

Report
of
Special Committee Advisory to
The Secretary of Health, Education, and Welfare
To Review the Policies, Procedures, and Decisions of
The Division of Antibiotics and the New Drug Branch of
The Food and Drug Administration

A. Mission - This Committee was appointed in June 1960 by the President of the National Academy of Sciences at the request of the Secretary of Health, Education, and Welfare. It was asked to review the policies and procedures used by the Food and Drug Administration in reaching decisions concerning the acceptance and certification of new drugs, including antibiotics, and the scientific soundness of the decisions made in recent years. The Committee was also invited to present such recommendations as it might consider desirable for the protection of the public health through the functions of the FDA.

B. Procedure - The Committee met on 28 June to plan its activities and again on 8 September to discuss its findings and formulate its recommendations. In both meetings it had the assistance of representatives of the Secretary's office and the FDA, who cooperated by providing pertinent information and answering questions arising from the study. The necessary legal steps were taken to permit members unrestricted access to the FDA files. In addition, an extensive file of documents concerning the law and regulations, policies and procedures, staffing and organization, and other pertinent matters was forwarded to each member for background and reference. (A list of these documents is appended.)

It was at once apparent that the Committee could not hope in any reasonable period to examine all, or even a large proportion, of the thousands of voluminous applications for certifiable antibiotic preparations and new drugs processed under the Federal Food, Drug, and Cosmetic Act in recent years. It was therefore decided that the members would select for detailed study a limited number of preparations which they considered to be of especial significance. In all, 29 applications were reviewed, covering 3 preparations of certifiable antibiotics, 14 of antibiotics classed as new drugs, and 12 of other new drugs.

C. Conclusions - While the proportion of decisions studied was necessarily small, the Committee believes its sampling to be sufficiently representative, particularly of preparations which have been the subject of some controversy, to provide a reasonable basis for conclusions as to the performance of the FDA staff in protecting the public health.

Taking into account the limitations of the FDA's authority, funds, and scientific personnel, the Committee found the decisions it reviewed acceptable, despite certain deficiencies in the quality and quantity of the data upon which they were based. It found no evidence of disregard for the public health, and noted that appropriate action had been taken when hazards were established by subsequent clinical experience.

Nevertheless, the Committee concluded that certain weaknesses inherent in the existing law and current staffing and budgetary support hamper the FDA in its task of protecting the public health. Accordingly, it has addressed its recommendations primarily to the correction of these defects. The increasing rate at which medical research is expanding and new and powerful drugs are being developed is multiplying the number of potential hazards to be controlled. Therefore, the Committee believes it essential that these recommendations be acted upon with the least possible delay.

D. Recommendations -

1. The FDA should be given statutory authority to require proof of the efficacy, as well as the safety, of all new drugs. Treatment of a patient with an ineffective drug in place of an effective one may jeopardize his recovery. This is true even though the drug may not be intrinsically harmful, and even though the specific condition for which the drug is given may not be ordinarily regarded as life-threatening.

2. The FDA should be given statutory authority to require manufacturers of new drugs to maintain records and submit reports of clinical experience and other relevant data, not only before but after the drug is released for sale, as requested by the Commissioner in his proposed Factory Inspection and Drug Amendments of 1960. Any evaluation of a new drug is subject to revision in the light of broader experience, and the FDA must be in a position to advise the profession and warn the public promptly whenever new hazards are revealed.

3. The FDA should be given statutory authority to apply certification procedures to all antimicrobial agents used in the prophylaxis and treatment of infectious diseases. The Committee sees no reason for limiting certification to those antibiotic preparations which happen to have come on the market prior to 1950, and further believes that all agents employed for equally serious conditions should be subject to equivalent measures of control.

4. The Committee recognizes the importance to the public health of ensuring that all drugs are prepared under the highest standards of quality control. It therefore endorses the Commissioner's proposals in the Factory Inspection and Drug Amendments of 1960 to clarify and strengthen existing inspection authority, and to require that all drugs be manufactured and packaged under adequate controls.

5. The Committee believes that the information supplied to physicians concerning drugs should be not only accurate, but also complete, and that the date of such information is essential to its proper evaluation. It therefore endorses the proposed amendments to present labeling requirements published by the Commissioner in the Federal Register for 22 July 1960.

6. The Committee considers that the advertising of pharmaceuticals requires more careful regulation than that of products unrelated to the prevention and cure of disease. It therefore recommends that careful study be given to the problem of coordinating the supervision of labeling, promotional material, and other advertising of drugs, now divided among several agencies of the Government, and to means of ensuring that all information concerning drugs conveyed to the profession and the public by whatever media be in conformity with scientific fact.

7. When a decision has been reached concerning an application, a statement should be prepared and incorporated in the file summarizing the conclusions, the names and opinions of those involved, and such other data as may be necessary to provide a concise record of the basis for the decision. This should be of great assistance in the administrative review of current actions and in the scientific review of the files in relation to subsequent applications, as well as when the advice of consultants is sought.

8. The staff members responsible for processing applications should be supported to the utmost in their efforts to obtain submission of truly dependable scientific information on the efficacy and safety of the products. The data initially submitted by the manufacturer are not always of sufficient quality and quantity to permit a sound decision as to the merits of the product.

9. The FDA should be strongly supported in its effort to maintain a research program of high quality on the methodology and standardization of drug testing and related areas of basic science. This is important not only to improve the methods available for carrying out its responsibilities to the public, but also as an aid in recruiting and retaining competent scientists on the staff.

10. The Committee urges the Commissioner to seek such authorization as may be necessary to establish an advisory organization of scientific and technical experts as a recognized resource for advice on criteria, procedures, and policies for the execution of the responsibilities of the FDA.

11. It is recognized that these various recommendations cannot be carried out without expanded resources, both of funds and of personnel. The Committee also considers that the present resources of the FDA are less than adequate to meet existing responsibilities. It therefore urges that the FDA be granted the authority and funds required to employ and retain larger numbers of highly qualified personnel and to support their activities, and endorses the recommendations made to this end by the Citizens' Advisory Committee in 1955.

Approved 27 September 1960

MEMBERS OF COMMITTEE

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BACKGROUND MATERIAL FURNISHED BY FDA TO MEMBERS OF SPECIAL COMMITTEE

1. Material for NRC Committee - Certification of Antibiotics, 20 June 1960

   A. Federal Food, Drug, and Cosmetic Act (Exhibit A)
   B. Organization, Division of Antibiotics (Exhibit B)
   C. Organization, Antibiotics Branch, Bureau of Medicine (Exhibit C)
   D. Antibiotics Regulation, Vol. I (Exhibit D)
   E. Antibiotics Regulation, Vol. II (Exhibit E)
   F. Operations of the Division of Antibiotics (Exhibit F)
   G. Research in the Division of Antibiotics (Exhibit G)
   H. Reprints of various publications (Exhibit H)
   I. Curriculum Vitae of Dr. Welch (Exhibit J)

2. Types of Decisions Involved in Establishing Antibiotic Regulations, 23 June 1960 (Certifiable Antibiotics only)

3. Memorandum, Background Information for the NAS Committee, 22 June 1960, from Dr. W. H. Kessenich, Medical Director, Bureau of Medicine, with attachments:

   A. Federal Food, Drug, and Cosmetic Act
   B. General Regulations for the Enforcement of the Federal Food, Drug, and Cosmetic Act
   C. New Drug Regulations (Encl. 2)
   D. New Drug Application Form (Encl. 3)
   E. Statement of George P. Larrick (Encl. 4)
   F. Organization Chart of FDA and Bureau of Medicine (Encl. 5)

4. Memorandum, Background Information for the NAS Committee from Bureau of Medicine, 28 June 1960

5. New Drug Applications handled during period January 1958 - March 1960

6. Staffing Pattern, FDA - 1 July 1960

7. Report of Citizens' Advisory Committee on FDA, dated June 1955

8. Pamphlet, "Protecting Consumers of Food, Drugs, Cosmetics", dated 15 October 1959

9. Report of Panel on Food Additives, dated 9 May 1960

10. "Factory Inspection and Drug Amendments of 1960" - Press release dated 1 July 1960, Bill and Amendment

Comments by the Secretary of Health, Education, and Welfare, Arthur S. Flemming, on the Recommendations of the Special Advisory Committee to Review the Policies, Procedures and Decisions of the Division of Antibiotics and the New Drug Branch of the Food and Drug Administration

Recommendation	Comments
1	I concur in this recommendation that FDA be given statutory authority to require proof of the efficacy, as well as the safety, of all new drugs. There are now two significant concepts on the basis of which the Food and Drug Administration does, in fact, require a demonstration of the efficacy of new drugs before applications are cleared, namely, (1) when the drug is offered for the treatment of a life-threatening disease, and (2) when the drug may have a definite potentiality to do harm where we have to measure the good the drug does against its possible hazards. But I agree that the new drug procedures are not adequate to insure the efficacy of drugs which are essentially innocuous. Commissioner George P. Larrick testified before the Senate Subcommittee on Antitrust and Monopoly on June 3, 1960, as follows: "We would endorse a proposal that the new drug section of the Food, Drug, and Cosmetic Act require a showing of efficacy as well as a showing of safety."
2	I concur in this recommendation that the Food and Drug Administration be given statutory authority to require manufacturers of drugs to maintain records and submit reports of clinical experience, particularly

Recommendation	Comments
	after the drug is released for sale. Senate Bill 3815 introduced in the 86th Congress, 2d Session, specifically provides for such recordkeeping and reporting. The Department of Health, Education, and Welfare submitted this bill as a proposal to Congress to strengthen the Federal Food, Drug, and Cosmetic Act.
3	I concur in this recommendation that FDA be given statutory authority to apply certification procedures to all antimicrobial agents. The present law now provides for certification for products composed wholly or partly of any kind of penicillin, streptomycin, chlortetracycline, chloramphenicol, or bacitracin or any derivative thereof. Recommendation 3 would extend mandatory certification procedures to all antimicrobial agents whether produced by living microorganism or by any other means.
4	I concur in this recommendation that the inspection authority be strengthened to require that all drugs be manufactured and packaged under adequate controls. S 3815, proposed by the Department of Health, Education, and Welfare, specifically provides that drugs be produced under adequate controls and manufacturing processing, packaging and storing, or be deemed to be adulterated within the meaning of the Act.

Recommendation	Comments
5	I concur in this recommendation that the information supplied to physicians concerning drugs be accurate and complete. The proposed revisions in the regulations under Section 502(f)(1) as published in the Federal Register for July 22, 1960 will aid--as far as the Food, Drug, and Cosmetic Act will permit--in the control of false and misleading promotion of new drugs to the medical profession.
6	The issue reflected in this recommendation is an important one. I am asking that a careful study be made of the organizational problems involved and, when this study has been completed, I will make recommendations to the President.
7	I concur in this recommendation that a concise record be prepared for the file summarizing the basis on which the decision is made to permit a new drug application to become effective. I have asked Commissioner Larrick to submit proposals to me as to what needs to be done to carry out this recommendation.
8	I concur in this recommendation that the staff members responsible for processing new drug applications be supported fully in their insistence that they receive complete and dependable scientific data to support new drug applications. This Department is aware of its enormous responsibility in the clearance of new

Recommendation	Comments
	drugs and antibiotics, and it recognizes the importance of and need for comprehensive competent scientific data and information on the safety and efficacy of new drugs. I shall continue to insist upon the fullest submission of safety and efficacy data necessary for intelligent study and evaluation of new drug applications.
9	I concur in this recommendation that FDA should have a sound research program on methodology and drug testing. Such a research program is an essential part of the Food and Drug Administration's effort to improve its enforcement operations. We recently increased our work in this area and plan to broaden it still further.
10	I concur in this recommendation that the Commissioner of Food and Drugs seek authority to establish an advisory organization of scientific and technical experts. The complexity of present day new drugs and the constant flow of progress and new developments in the drug field makes it essential that the Food and Drug Administration have for its guidance the most competent scientific resources available in the United States. I have asked Commissioner Larrick to make appropriate proposals to me for the implementation of this recommendation.

Recommendation	Comments
11	I concur in this recommendation that FDA needs expanded resources support. Without adequate resources of both funds and personnel the great responsibilities imposed upon the Food and Drug Administration cannot be met. I anticipate increased recognition of this fact.

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EXHIBIT 2

Letter from Council on Drugs of American Medical Association

May 22, 1961

Dear Doctor:

We should greatly appreciate your serving as a consultant assisting the Council on Drugs in its evaluation of ....

We realize that you have many demands on your time, but feel that you may wish to assist us in the evaluation of this agent in particular since the manufacturer has used a general comment of yours as a reference in what may or may not be a misleading fashion in the product brochure.

There is enclosed a collection of data, reprints, and summaries of published papers supplied by the manufacturer. You will render invaluable assistance to the Council by reviewing this material and providing us with your assessment and evaluation of the drug... Your comments are especially invited concerning the adequacy of the laboratory and clinical data, usefulness, indications and contraindications and toxicity of the drug; comparisons with other similar drugs would also be helpful...

Each drug description is designed to provide fair comment and criticism based on available evidence, whether or not this is considered adequate to establish usefulness. Thus, the monographs may be either favorable or unfavorable.

EXHIBIT 3

Washington, D.C.
December 23, 1960

Honorable Arthur S. Flemming
Secretary of Health, Education, and Welfare
Washington 25, D.C.

Dear Mr. Secretary:

I am happy to submit herewith the report of the Special Investigative Unit appointed by you last June to look into certain charges involving employees and operations of the Food and Drug Administration.

The opinions expressed are the joint and several opinions of the members of the Unit, without dissent. I trust that you will find them helpful.

The other members of the Unit have authorized me to express our appreciation for the very fine cooperation of the many persons upon whom we had to call for help, from your own office, Mr. Miles' office, the General Counsel's office and the entire Food and Drug Administration. We also wish to thank you for the expression of confidence in us which is implicit in the assignment.

Sincerely yours,

/s/

Charles H. Kendall

Enclosure

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